

Type 1 Diabetes TrialNet

Long-term Investigative Follow-up in TrialNet (LIFT)

Type 1 Diabetes TrialNet

Researchers in this study are part of a larger group called Type 1 Diabetes TrialNet. TrialNet is an international network of centers dedicated to the study, prevention, and early treatment of type 1 diabetes. We have clinical centers in the United States, Canada, Europe, and Australia.

We are conducting studies to:

- Learn more about the common risk factors among people who get type 1 diabetes.
- Test treatments that could help delay or prevent the start of type 1 diabetes.
- Test treatments that might help people who have recently been diagnosed with diabetes keep producing their own insulin.

TrialNet is supported by:

[DHHS, NIH, NIDDK, NIAID, NICHD, NCRR, JDRF, ADA logos]

To learn more about type 1 diabetes studies or to get a referral to a TrialNet study, call toll free 1-800-HALT-DM1 (1-800-425-8361). You can also learn more about TrialNet at www.DiabetesTrialNet.org.

Clinical Center: _____

Research Physician: _____

Study Coordinator: _____

Tel: _____

Fax: _____

E-mail: _____

Affiliate Center: _____

Research Physician: _____

Study Coordinator: _____

Tel: _____

Fax: _____

E-mail: _____

You were in a TrialNet study. You helped us learn more about type 1 diabetes. We hope you will help us keep learning by joining this long-term, follow-up study.

After you read this handbook, we will talk with you about the study and answer your questions. We will ask you to sign a consent form if you decide you want to join the study.

As you make your decision:

- * Ask questions. We want to answer all your questions and talk about any concerns you have.

- * Talk about the study with your family doctor. Your doctor is welcome to call us with questions.
- * Talk to your family and friends.

As a research volunteer, you can decide to leave this study at any time. We hope that you will stay in the study. You will be helping us learn more about how to help people with diabetes.

BACKGROUND

Cells in the pancreas, called beta cells, make insulin. In type 1 diabetes, the immune system slowly destroys the beta cells. This goes on for years.

When many of the beta cells are gone, blood glucose levels go too high. At this point, the person has diabetes but doesn't have symptoms yet. Some people call this "silent diabetes."

The immune system keeps destroying beta cells. Blood glucose levels go higher, and the person shows symptoms of diabetes. Even so, the person may still be making some insulin. But the immune system keeps attacking the beta cells. A few years after diagnosis, most people are secreting little to no insulin of their own.

WITH YOUR HELP WE HOPE TO LEARN MORE ABOUT DIABETES

➤ If you were in the Natural History Study or a TrialNet prevention study:

You are very important to this study. You can help us fill in some gaps in our knowledge about how diabetes develops.

- * What happens in the body in the months just before and just after a person develops diabetes?
- * Does starting insulin treatment at an early stage make a difference over the long run?
- * Does a treatment we tested in a prevention study have an effect during that first year of diabetes, and even beyond?
- * Are there any long-term effects—good or bad—from the treatments in these studies?

➤ If you were in a TrialNet new onset (intervention) study:

You are done with your follow-up visits for the intervention study. We would like to do long-term follow-up.

- * Are there any long-term effects—good or bad—from the treatments in these studies? It's important for us to follow up with everyone in the studies.
- * Are there any differences in diabetes control between the people who got the experimental treatments and those who did not?

TESTS IN THIS STUDY

Many of the tests in the LIFT Study are the same ones you had in your other TrialNet study.

A1C: The Test with a Memory

An A1C test (also called hemoglobin A1c or HbA1c) shows your average blood glucose level over the past 2 to 3 months.

When blood glucose levels are high, extra glucose attaches to red blood cells. A blood test done weeks or even two or three months after blood glucose was too high will show that the red blood cells have extra glucose attached. That's why the A1C is called the test with a memory.

In someone who does not have diabetes, the A1C level will be less than 6.5%. Talk to your regular doctor about what your goal is.

In this study, we will draw blood to test your A1C at every visit.

C-peptide: How Much Insulin You Make

To measure how much insulin your body secretes, we test your blood for **C-peptide**.

When the body makes insulin, it first makes a long protein molecule called proinsulin. This splits into two pieces. The larger piece is an insulin molecule. The smaller piece is C-peptide. There is no C-peptide in injected insulin. **So when we measure your blood for C-peptide, we see how much insulin your body secretes.**

One study showed that people with type 1 diabetes who have higher levels of C-peptide tend to have better blood glucose control, fewer problems with low blood glucose reactions (hypoglycemia), and fewer long-term diabetes complications than people who have no C-peptide.

In this study, we will measure C-peptide at a visit every 6 months, by doing an oral glucose tolerance test (OGTT) and/or a mixed meal tolerance test (MMTT).

We will tell you what your peak C-peptide level was soon after each test. Even though your C-peptide levels may go up sometimes and then down again, we expect your C-peptide levels to go down over time. When our tests can no longer detect C-peptide, you will switch to annual visits, and have no more tests for C-peptide.

Other Blood Tests

One goal of TrialNet is to learn more about diabetes and autoimmune disease. To do this, we might take blood samples for studies by TrialNet-approved researchers. These studies may include tests of genes and how they work as well as tests of the immune system and other cells in the body. Some samples might be used right away by TrialNet-approved researchers and some stored for future use by TrialNet approved researchers.

With your permission, once TrialNet is over, some samples might be stored for future use by other researchers. You will give permission for this on the Informed Consent you sign before any blood is drawn. The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) will be responsible for these samples. Once TrialNet is completed, researchers from outside TrialNet can ask for stored samples from NIDDK. The samples will be labeled only with an ID number. Since there is no longer any link to you, we would not be able to remove your stored samples.

Urine Tests

We might need to do other tests in the future. For example, we might do urine tests to check for any long-term effects of experimental treatments used in other TrialNet studies.

RISKS AND DISCOMFORTS

You could have discomfort and/or a bruise when you get your blood drawn. Some people may faint. It is rare, but some people may get an infection, a small blood clot, swelling of the vein and surrounding tissue, or bleeding at the needle puncture site.

Some people don't like the taste of the drinks used in the OGTT and MMTT, or it makes them feel sick to their stomachs.

CALL US

Call us if you have any questions or concerns about the study.

Please let us know if you don't want to be in the study any longer. You or your child are always free to stop being in the study. Your future medical care will not be affected in any way.

SCHEDULE OF VISITS

IF YOU CAME FROM TRIALNET NATURAL HISTORY OR A PREVENTION STUDY

What to expect at semi-annual visits (C-peptide still present)

Until you reach the first year after diagnosis of diabetes, the test for C-peptide will be either an OGTT or an MMTT.

At the visit one year after your diagnosis, if you still have C-peptide, you will do both an OGTT and an MMTT. We have to do the tests on different days. We know it's a lot to ask of you. If you don't want to have both tests, we will ask to do just the MMTT at the one-year visit.

After one year, if you continue to have C-peptide, you will just continue to do the MMTT every six months.

The OGTT measures how your body responds to carbohydrate. The MMTT measures how your body responds to carbohydrate, fat, and protein. For many years, researchers have used OGTT before diagnosis and MMTT after diagnosis. You are in the transition time. Doing both tests on you may give us important information about the first year of diabetes.

Sometimes, a person shows no C-peptide on an OGTT, but shows some on an MMTT.

- If you show no C-peptide on an OGTT, we will not do any more OGTTs. We'll do an MMTT at your next visit.
- If you show no C-peptide on an MMTT, we will stop measuring C-peptide. You will switch to annual visits. See below for more information on annual visits.

For semi-annual visits (when having OGTT and/or MMTT), all tests are fasting (no food or beverages except water after 10 pm) and you should allow at least 3 hours for the visit.

- At every visit, we will draw blood. The volume of blood that we draw will always be safe for your age and weight.
- We will test for C-peptide. See p. **XX** for how to prep for the OGTT or MMTT.
- We will do an A1C test.
- We may also take blood samples that we will store and use later in other studies to learn more about type 1 diabetes.
- At some visits, we may draw extra blood to make sure the results are accurate.
- We will ask about your diabetes and general health.
- We may do a limited physical exam if the study doctor feels it is needed.
- We may ask for a urine sample.

What to expect at annual visits (C-peptide no longer present)

For all visits you will have blood drawn. You will not need to go without food or water and should allow 30-60 minutes for the visit.

- We will do an A1C test.
- We will ask about your diabetes and general health.
- We might ask for a urine sample.
- We might draw blood for other tests. It depends on which TrialNet study you were in before. We will talk to you more about this.

IF YOU CAME FROM TRIALNET INTERVENTION STUDY

- If your last MMTT showed C-peptide was present, you will come to a TrialNet Clinical Center for visits **every 6 months**.
- If you were negative for C-peptide on your last MMTT, you will switch to **annual visits**.

What to expect at semi-annual visits (C-peptide still present)

- At every visit, we will draw blood. The volume of blood that we draw will always be safe for your age and weight.
- We will do an MMTT to test for C-peptide. See p. **XX** for how to prep for these tests.
- We will do an A1C test.
- We may also take blood samples that we will store and use later in other studies to learn more about type 1 diabetes.
- At some visits, we may draw extra blood to make sure the results are accurate.
- We will ask about your diabetes and general health.
- We may do a limited physical exam if the study doctor feels it is needed
- We may ask for a urine sample.

What to expect at annual visits (C-peptide no longer present)

- We will do an A1C test.
- We will ask about your diabetes and general health.
- We might ask for a urine sample.
- We might draw blood for other tests. It depends on which TrialNet study you were in before. We will talk to you about this.

BEFORE YOUR OGTT AND/OR MMTT

Insulin Plan

We will tell you how to change your insulin plan the day before and the day of the test.

Medicines

Call us if you're taking any prescription or over-the-counter medicine that you haven't told us about before. Some medicines may change the test results.

Eat plenty of starches and sugar.

Eat at least 150 grams of carbohydrate (starches and sugars) a day for at least **three days** before the test. Most adults and children eat 150 grams or more in a usual day, so this will probably not mean a new diet for you. Eating more than 150 grams of carbohydrate is OK.

Foods with carbohydrate include:

- Grains: breads, pasta, crackers, cereals (hot and cold)
- Beans
- Starchy vegetables: potatoes, peas, corn
- Fruit: fresh, canned, dried, juices
- Milk (whole, 2%, 1%, non-fat, chocolate), yogurt

Each of these has about 15 grams of carbohydrate:

1 slice of bread	1/3 cup rice
6 crackers	1 cup low-fat milk
1/2 cup pasta	1 medium apple

Meat, cheese, and non-starchy vegetables (leafy greens, broccoli) have little or no carbohydrate. You can have these foods in the amounts that you normally eat.

Drink plenty of water the day before and the day of the test.

It will be easier for us to draw blood for the test.

For 10 hours before the OGTT or MMTT:

Have no food or drink other than water.

This includes:

No coffee or tea

No alcohol

No diet sodas or sugar-free gum. They have no calories, but the flavor can prompt your body to make insulin. This could change the test results.

Don't use tobacco.

Don't smoke or chew tobacco or use nicotine products.

Don't exercise.

Get a good night's sleep.

Don't schedule the test for the morning after you work a night shift.

HOW TO PREPARE FOR YOUR OGTT AND MMTT

Test Prep

- We may offer a numbing cream.
- We insert a needle into a vein in your arm or hand. We remove the needle, leaving a small plastic tube in your vein. This is called an intravenous (IV) line. We draw all the blood samples from this line.

The Test

- We will draw blood samples at the beginning of the test.
- For the OGTT, you drink about a cup (less for children) of a sweet drink. You have to drink it all in 5 minutes. Some people feel a little sick to their stomachs (nauseated) when they drink this.
- For the MMTT, you drink Boost, a liquid meal that tastes like a milkshake. It has carbohydrate, protein, and fat. You have to drink it all in 5 minutes.
- We will draw blood samples for 2 hours after the drink.
- You need to sit quietly or rest in bed during the test.

FREQUENTLY ASKED QUESTIONS

“How long will I be in the LIFT Study?”

We plan to keep the LIFT Study running for years. It is your choice to be in the study. You can stop being in the study at any time.

“If I am pregnant, can I be in the study?”

You can still be in the study, but you won't come in for study visits or have any blood tests for the study while you are pregnant. None of the testing will hurt your baby if done during pregnancy but some of the results may not be accurate for our purposes. If you find out after a visit that you were pregnant at the time of the visit, please let us know.

“If I start out coming every six months, will I stay on that schedule?”

When your MMTT is negative for C-peptide, you'll switch to annual visits. We don't know when this will happen. It's one of the things we will learn in this study.

“What are the benefits of being in the study?”

* **A1C results:** Your regular doctor will be testing your A1C. You and your doctor may find it helpful to have extra A1C results.

* **C-peptide results:** Doctors don't routinely test C-peptide levels. In this study, we will tell you what your peak C-peptide levels were after every OGTT or MMTT. Some people like to know if they are still making insulin.

* You will help us learn more about type 1 diabetes. This may help people in the future.